

## Article

# Gait Characteristics of Age-Related Macular Degeneration Patients

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**Purpose:** To identify potential differences between age-related macular degeneration (AMD) patients and controls in fall-relevant gait characteristics.

**Methods:** Spatiotemporal gait characteristics using the GAITRite walkway were collected from 29 AMD patients and 20 controls, aged 60 to 90 years, at the Wilmer Eye Institute. Multiple linear regressions, controlling for age, sex, body mass index (BMI), and comorbidities were used to assess associations between gait characteristics and AMD.

**Results:** Study participants were predominantly white (86%) and female (55%). Mean age of the full study population was 73.51 (SD: 8.14) years, and mean BMI was 27.80 (SD: 5.44) kg/m<sup>2</sup>. Median better-eye acuity (logMAR) was 0.23 (interquartile range [IQR] = 0.18, 0.36) and  $-0.02$  (IQR =  $-0.08$ , 0.02), while median binocular log contrast sensitivity was 1.44 (IQR = 1.32, 1.56) and 1.76 (IQR = 1.76, 1.80) for the AMD and control groups, respectively. In multivariable regression models, AMD patients had significantly slower walking speeds ( $\beta = -0.118$  m/sec [95% confidence interval (CI):  $-0.229$ ,  $-0.007$ ],  $P = 0.038$ ) and stride velocities ( $\beta = -0.119$  m/sec [95% CI:  $-0.232$ ,  $-0.007$ ],  $P = 0.038$ ), and greater double support time ( $\beta = 3.381\%$  of the walk cycle, 95% CI = 1.006, 5.757,  $P = 0.006$ ) than controls. There were no group differences in base of support, step length, stride length, or gait variability measures.

**Conclusion:** AMD patients exhibited many fall-relevant gait characteristics.

**Translational Relevance:** The finding of fall-relevant gait characteristics suggests that AMD patients may be at a greater risk of falls during ambulation than those without AMD.

## Introduction

Aging and vision impairment (VI) are both associated with a greater risk of falls. In the visually impaired, this higher fall risk is related to increased difficulty assessing hazards, ascertaining distance appropriately, and discerning spatial relationships<sup>1,2</sup> secondary to reduced visual acuity (VA), impaired visual fields (VF), and/or contrast sensitivity (CS).<sup>3</sup> In the elderly, falls are linked to an age-related decline in sensory and motor functions<sup>4</sup> and can result in significant morbidity, long-term disability and premature death.<sup>5</sup>

Given that age-related macular degeneration (AMD) is a disease of the elderly and is a leading cause of VI in this demographic, with 12% of the US

population over the age of 80 years<sup>6</sup> being affected by AMD, its relationship with mobility issues and falls has undergone considerable scrutiny.<sup>7,8</sup> Prior research has found AMD to be related to impaired physical functioning, with reduced CS and VA associated with increased rates of falls and other injuries.<sup>9,10</sup> Loss in central vision, a key component of AMD, has also been demonstrated to be an independent risk factor for falls.<sup>11</sup> Up to two-thirds of AMD patients struggle with balance from scotomas blocking central vision and attendant visuomotor deficits.<sup>12</sup> Also, as AMD severity increases, postural instability has been shown to be greater,<sup>13</sup> and poor balance has been postulated to be a significant factor affecting falls in these patients.

Apart from the harms associated with falls, there is the additional impact of self-imposed restriction of

physical activity in patients with AMD. Existing literature suggests that patients with VI from AMD are less likely to be mobile<sup>14</sup> or engage in physical activity,<sup>15</sup> and these restrictions can have significant impacts on physical, social, and mental well-being.<sup>16</sup> Research aimed at understanding ambulatory gait characteristics in AMD is paramount to increasing mobility, safety, quality of life, and the maintenance of independence in these older adults by aiding the preservation and/or improvement of this function.

Earlier studies have extensively investigated mobility performance in AMD subjects using walking courses<sup>8,17–19</sup> with some finding decreased travel speed and increased travel time to be associated with the disease. Despite this wealth of research, examination of the actual gait characteristics underlying these impaired mobility measures is limited. Spaulding et al.<sup>7,20</sup> and Wood et al.<sup>13</sup> both found that those with AMD have slower walking speeds and shorter stride lengths, indicating the use of greater caution during ambulation by AMD subjects than those with normal vision. We sought to build on this limited literature by exploring a broader array of gait characteristics, which have not been previously studied as allowed by the electronic gait mat, including the effect of AMD on stride-to-stride variability in gait parameters given prior data underlining its relevance to falls.<sup>21–23</sup>

To this end, we conducted a cross-sectional pilot study comparing spatiotemporal gait characteristics in older adults with at least some degree of VI from AMD to visually normal controls to evaluate how their gait characteristics might differ possibly putting those with AMD at a greater risk for difficulty with mobility and falls.

## Methods

This study was approved by the Johns Hopkins Medicine institutional review board and adhered to the tenets of the Declaration of Helsinki. It was conducted between August 2015 and May 2016, and informed written consent was obtained from participants after explanation of the nature of the study and prior to any study procedures. Trained research personnel conducted all study testing.

### Study Participants

Two study groups were recruited: AMD cases and glaucoma suspect controls followed at the retina and glaucoma clinics at the Wilmer Eye Institute, respectively. All study participants were between the ages of

60 and 90 years at time of enrollment with the ability to walk without the aid of any mobility device (wheelchair, walker, etc.) Patients with a history of an intravitreal injection 7 days prior, ocular surgery 4 weeks prior, and/or any nonocular surgery 3 months prior to testing were excluded. For the AMD group, subjects had (1) a chart diagnosis of dry (atrophic) or wet (exudative) AMD, and (2) Early Treatment Diabetic Retinopathy Study (ETDRS) best-corrected VA (BCVA) worse than 20/32 but better than 20/100 in the better-seeing eye, as the focus of this study was on mild to moderate vision loss from AMD. The control group came from visually normal subjects enrolled in the ongoing Falls in Glaucoma Study (FIGS), a longitudinal study also seeking to identify gait variables that relate to falls. Glaucoma suspects visiting Wilmer were chosen as controls given that they did not have significant VI, essentially being equivalent to visually normal controls, while still being comparable to the AMD group for hard-to-define reasons that people seek care at Wilmer. Controls had (1) a chart diagnosis of glaucoma suspect, (2) no AMD or any other ocular condition that could potentially impair vision, (3) ETDRS BCVA of 20/32 or better in both eyes, and (4) the following VF criteria on SITA standard 24-2 testing: (1) mean deviation (MD) better than  $-3$  decibels (dB) in at least one eye and (b) better than  $-5$  dB in both eyes, and (3) a normal/borderline glaucoma hemifield test (GHT).

### Evaluation of Gait (Outcome)

Gait data were collected via the GAITRite Electronic Walkway (CIR System Inc., Franklin, NJ) that has been shown to be a valid and reliable tool for automated gait analysis.<sup>24</sup> This system uses a “carpet” walkway that captures temporal and spatial gait parameters across an active area of  $0.61 \times 4.88$  m containing a grid of  $48 \times 384$  sensors. Gait measurements were collected as patients walked barefoot in a well-lit room making a total of four passes across the mat. The gait parameters measured were:

1. Base of support width: perpendicular distance (in meters) between the heel of the right leg and the line of progression created by heel strikes of the left leg;
2. Step length: the distance along the forward-backward axis (in meters) between the heel center of the right leg and the subsequent heel center of the left leg;

**Table 1.** Population Characteristics

Demographics	Total (N = 49)	Cases (N = 29)	Controls (N = 20)
Age, mean (SD), y	73.51 (8.14)	77.58 (6.46)	67.6 (6.60)*
Caucasian, n (%)	42 (85.71)	28 (96.55)	14 (70.00)*
Female, n (%)	27 (55.10)	13 (44.83)	14 (70.00)
Years of education, mean (SD)	15.96 (1.65)	15.86 (1.79)	16.10 (1.45)
Employed, n (%)	19 (38.78)	9 (31.03)	10 (50.00)
<b>Health</b>			
Body mass index in kg/m <sup>2</sup> , mean (SD)	27.80 (5.44)	26.83 (5.03)	29.21 (5.83)
Comorbid illnesses, mean (SD)	2.27 (1.72)	2.31 (1.56)	2.20 (1.96)
Polypharmacy ≥ 5 meds, n (%)	23 (46.94)	17 (58.62)	6 (30.00)*
MMSE score, mean (SD)	20.49 (1.52)	20.31 (1.65)	20.75 (1.65)
Self-reported difficulty with ≥ 1 IADL, n (%)	19 (38.78)	14 (48.28)	5 (25.00)
<b>Vision</b>			
Better-eye visual acuity, in logMAR, median (IQR)	0.1 (0, 0.24)	0.23 (0.18, 0.36)	−0.02 (−0.08, 0.02)*
Worse-eye visual acuity, in logMAR, median (IQR)	0.30 (0.06, 0.49)	0.42 (0.33, 0.56)	0.04 (0, 0.14)*
Binocular log CS, median (IQR)	1.64 (1.44, 1.76)	1.44 (1.32, 1.56)	1.76 (1.76, 1.80)*

\* Denotes difference from cases at  $P < 0.05$ . SD, standard deviation; MMSE, mini-mental state examination; IADL, instrumental activities of daily living; IQR, interquartile range; CS, contrast sensitivity.

3. Stride length: the distance (in meters) between the heel centers of two consecutive footprints of the right leg;
4. Walking speed: the total distance travelled (in meters) divided by the time taken to do so (in seconds);
5. Stride velocity: the stride length (in meters) of the right leg divided by the stride time (in seconds); and
6. Double support time: percentage of time spent with both feet on the mat.

### Evaluation of Vision

Unocular and binocular VA was measured using ETDRS charts backlit at 130 candelas/m<sup>2</sup> with patients wearing their habitual distance correction. The total number of letters read correctly were converted to the negative logarithm of the minimum angle of resolution (logMAR)<sup>25</sup> for statistical analysis. Contrast sensitivity was measured uni- and binocularly using the MARS chart<sup>26</sup> under standardized distance (40 cm) and ambient light conditions.

### Evaluation of Covariates

Sociodemographic data, including age, race, education, and occupation were collected using standardized questionnaires. Variables pertaining to health (other health conditions and polypharmacy) were also

gathered using standardized forms. Patients were asked if they had any of 15 coexisting medical conditions known to affect mobility as previously listed.<sup>27</sup> They were also questioned regarding their current systemic prescription medication use (over the counter drugs and eye-disease specific medications were not included in analysis). The Mini-Mental State Exam (MMSE) adapted for the visually impaired<sup>28</sup> (maximum score of 22) was used to assess cognitive function. The presence of any difficulty with activities of daily living was assessed using the instrumental activities of daily living (IADL)<sup>29</sup> questionnaire, with a positive response to any question taken to indicate the presence of difficulty performing everyday tasks.

### Statistical Analysis

Differences in demographic, health, and vision characteristics between AMD and control groups were analyzed using Student's *t*-tests and  $\chi^2$  or Fisher's exact tests for continuous variables and categorical variables, respectively. VA in the better-seeing eye was used for all analyses. All gait parameters were continuous outcomes and data from the right leg was used to compare each outcome by AMD status, logMAR VA, and logCS using separate multivariable linear regression models adjusting for potential confounders, including demographic (age, sex, and race) and health specific (body mass index [BMI] and other health conditions) variables. Additional multi-

**Table 2.** Multivariable Linear Regressions Assessing Associations between Covariates and Gait Characteristics

	Gait Parameters		
	Walking Speed (m/sec) β 95%(CI)	Base of Support (m) β 95%(CI)	Step Length (m) β 95%(CI)
AMD <sup>a</sup> (vs. Control)	<b>-0.118 (-0.229, -0.007)</b>	0.007 (-0.011, 0.256)	-0.046 (-0.098, 0.007)
Better eye logMAR VA <sup>b</sup> (0.1 logMAR worse)	-0.014 (-0.039, 0.011)	-0.001 (-0.005, 0.003)	-0.008 (-0.019, 0.004)
Binocular log CS <sup>c</sup> (0.1 log units worse)	-0.006 (-0.026, 0.013)	0.001 (-0.003, 0.003)	-0.005 (-0.014, 0.005)

Bold font indicates  $P < 0.05$ . CI, confidence interval; AMD, age-related macular degeneration; VA, visual acuity; CS, contrast sensitivity; BMI, body mass index.

<sup>a</sup> Denotes model with covariates: group, age, sex, BMI, and other illnesses.

<sup>b</sup> Denotes model with covariates: better eye logMAR VA, age, sex, BMI, and other illnesses.

<sup>c</sup> Denotes model with covariates: binocular log CS, age, sex, BMI, and other illnesses.

variable linear regression models also adjusting for age, sex, race, BMI, and other health conditions were used to evaluate gait variability across the four walks for each outcome measure using the inter-stride coefficient of variation (CV) value, expressed in percentages. The CV is a measure of spread that describes the amount of variability in gait relative to the mean, and was calculated as the standard deviation (SD) divided by the mean and multiplied by 100.

MMSE score was categorized as a binary variable with a cut off at the median ( $\leq 20$  vs.  $> 20$ ), but neither MMSE nor IADL scores were used in the final model as adjusting for them yielded no significant changes in the gait estimates. Polypharmacy was defined as taking greater than or equal to five prescription medications by self-report based on previous literature<sup>30,31</sup> and coded as a binary variable ( $< 5$  vs.  $\geq 5$ ). Other health conditions variable was defined as the number of comorbid illnesses as reported by the patient and coded as a binary variable with a cut off at the median ( $\leq 2$  vs.  $> 2$ ). In order to avoid possible

over-controlling, we did not include polypharmacy in the final model and only retained other health conditions.

All analyses were performed using Stata Statistical Software, release 14.1 (StataCorp LP, College Station, TX). Statistical significance was set at a  $P$  less than 0.05.

## Results

Data from a total of 49 participants comprising 29 AMD cases and 20 glaucoma suspect controls were analyzed. AMD participants were older (mean [SD]: 77.6 [6.46] vs. 67.6 [6.60] years,  $P < 0.05$ ) than controls and more likely to be white ( $N = 28, 97\%$  vs.  $N = 14, 70\%$ ,  $P < 0.05$ ), but did not differ from them with regard to sex, education level, employment status, BMI, number of other illnesses, MMSE score, or IADL score ( $P > 0.05$  for all, [Table 1](#)). Frequency of polypharmacy was greater in AMD cases than controls (58.62% vs. 30.00%,  $P < 0.05$ ). Compared

**Table 3.** Multivariable Linear Regressions Assessing Associations between Covariates and Coefficients of Variations of Gait Characteristics

	Coefficients of Variation	
	Base of Support (%) β 95%(CI)	Step Length (%) β 95%(CI)
AMD <sup>a</sup> (vs. Control)	1.929 (-4.897, 8.757)	-0.390 (-2.263, 1.482)
Better eye logMAR VA <sup>b</sup> (0.1 log units worse)	0.250 (-1.269, 1.769)	0.064 (-0.353, 0.482)
Binocular log CS <sup>c</sup> (0.1 logMAR worse)	-0.039 (-1.277, 1.201)	-0.390 (-2.263, 1.482)

<sup>a</sup> Denotes model with covariates: group, age, sex, BMI, and other illnesses.

<sup>b</sup> Denotes model with covariates: better eye logMAR VA, age, sex, BMI, and other illnesses.

<sup>c</sup> Denotes model with covariates: binocular log CS, age, sex, BMI, and other illnesses.

**Table 2.** Extended

	Gait Parameters		
	Stride Length (m) β 95%(CI)	Stride Velocity (m/sec) β 95%(CI)	Double Support (%) β 95%(CI)
AMD <sup>a</sup> (vs. Control)	0.073 (−0.172, 0.025)	−0.119 (−0.232, −0.007)	3.381 (1.006, 5.757)
Better eye logMAR VA <sup>b</sup> (0.1 logMAR worse)	−0.013 (−0.035, 0.008)	−0.014 (−0.040, 0.114)	0.532 (−0.017, 1.081)
Binocular log CS <sup>c</sup> (0.1 log units worse)	−0.009 (−0.026, 0.008)	−0.007 (−0.027, 0.133)	0.199 (−0.238, 0.637)

with visually normal controls, AMD cases' worse VA was as follows: median better eye-VA interquartile range (IQR): 0.23 (0.18, 0.36) versus −0.02 (−0.08, 0.02)logMAR, and worse CS was as follows: median binocular log CS (IQR): 0.42 (0.33, 0.56) versus 0.04 (0, 0.14) log units), (*P* < 0.05 for both). Mean walking speed was 0.995 m/sec (SD: 0.190) in the control group and 0.866 m/sec (SD: 0.142) in the AMD group.

In separate multivariable regression models, all adjusted for age, sex, BMI, and other illnesses, the impact of AMD, VA, and CS on gait variables was analyzed (Table 2). When compared to controls, AMD cases had slower walking speed ( $\beta = -0.118$  m/sec [95% confidence interval (CI): −0.229, −0.007]), slower stride velocity ( $\beta = -0.119$  m/sec [95% CI: −0.232, −0.007]), and greater double support time ( $\beta = 3.381\%$  [95% CI: 1.006, 5.757]), (*P* < 0.05 for all). A pattern of association between shorter step lengths AMD status ( $\beta = -0.046$  m [95% CI: −0.098, 0.007], *P* = 0.086) that did not reach statistical significance was found. Similarly, a pattern of association between worse VA (per 0.1 logMAR) and greater double support time ( $\beta = 0.532$  [95% CI: −0.017, 1.081] %, *P* =

0.057) that did not reach statistical significance was seen.

Multivariable linear regression models used to assess the relationship between inter-stride CV values of gait characteristics and AMD status, VA, or CS showed no associations between those variables (*P* > 0.05 for all; Table 3).

## Discussion

In this pilot study population, AMD status was associated with slower walking speed and stride velocity, and greater double support time. However, it is possible that these findings may be largely related to the older age of the AMD group compared with the controls. While neither VA nor CS, evaluated as continuous measures, were associated with statistically significant differences in gait parameters, the model evaluating the relationship between VA, and greater double support time showed a pattern of an association. AMD subjects did not show any differences in inter-stride variability of gait patterns in comparison with controls.

Our results are in accord with previous studies by Spaulding et al.<sup>7,20</sup> examining gait in AMD that

**Table 3.** Extended

	Coefficients of Variation	
	Stride Length (%) β 95%(CI)	Stride Velocity (%) β 95%(CI)
AMD <sup>a</sup> (vs. Control)	−0.749 (−1.761, 0.262)	−1.280 (−2.921, 0.360)
Better eye logMAR VA <sup>b</sup> (0.1 log units worse)	−0.032 (−0.263, 0.199)	−0.005 (−0.375, 0.366)
Binocular log CS <sup>c</sup> (0.1 logMAR worse)	−0.749 (−1.761, 0.262)	−1.280 (−2.921, 0.360)

found that AMD was associated with slower stride velocity. Another study performed by Wood et al.<sup>13</sup> found that reduced CS in AMD was associated with slower walking velocity, and increased double-support time. While we report similar gait adaptations in our AMD cohort, our findings differ in that CS or other covariates in our study did not explain our results.

These changes noted in walking patterns, such as decreased walking speed<sup>32,33</sup> and greater double support time<sup>34</sup> have been previously associated with an increased risk of falling. It has also been postulated that these changes in gait parameters are indicative of stabilizing gait adaptations related to increased caution expressed by patients secondary to a fear of falling.<sup>35</sup> In fact, prior literature suggests that a slower walking velocity is a compensatory mechanism adopted secondary to an effort to increase postural stability in the elderly.<sup>13,36</sup> Our results suggest that AMD subjects have certain gait characteristics that may contribute to mobility issues; however, we did not specifically test the role of past falls, fear of falling, or assess falls prospectively.

This study adds to the limited body of existing literature on gait parameters in AMD and is one of only three studies providing detailed three-dimensional kinematic gait analysis. Additionally, this is the first study to examine stride-to-stride CV in gait characteristics in AMD. However, this study has some limitations.

First, we tested gait under simple walking conditions alone. Research assessing the effect of AMD on walking under more challenging settings, such as extreme ambient lighting, courses with obstructions, and uneven terrain, such as the those studies conducted by Spaulding et al.<sup>7,20</sup> will provide more robust data helping understand gait under “real world” settings.

A second concern is the unequal age and sex distributions between our groups, with the control group being close to a decade younger and having a larger proportion of females than the AMD group. While we controlled for age and sex in our analysis, a more balanced distribution in these demographics between groups may have provided more optimal precision to our effect measures. Additionally, because AMD cases were substantially older than the controls, our results should be interpreted with caution, as it is possible that our findings might not be due to AMD itself, but rather the considerably older age of the AMD group. Limited resources precluded recruitment of more appropriate controls

outside our clinic but it might be worthwhile for future studies to attempt wider recruitment of more elderly, age-matched controls.

Finally, the study might have benefited from additional testing and collection of information on history of falls, handedness/footedness, and VFs. Information on foot dominance was not obtained and we uniformly analyzed right leg data. Using data from the dominant limb that is preferentially used for performance of mobilization tasks might be a better indicator of gait than data from the same limb in all subjects. Furthermore, because we did not perform VF testing, we could not investigate the effects of a central scotoma on gait. Similarly, past falls and/or fear of falling experienced by our participants might have been important factors to consider as they may have influenced their gait making those who are fearful adopt more cautious gait patterns.

In summary, we conclude that patients with AMD have slower walking speeds and stride velocities, and spend a greater proportion of time with both feet on the ground while walking, compared with controls, and that these gait characteristics could potentially result in mobility difficulties and increased fall risk in AMD. Maintenance of the ability of independent and safe ambulation is important to physical and psychosocial well being, and our research supports the need for further evaluation of gait and variability in gait in AMD in studies with larger populations, and a longitudinal design allowing the examination of adaptation of gait as it develops. It would also be useful to examine if the adoption of any stabilizing adaptations actually results in a lower risk of falls.

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